Remarks

Claims 1-13 and 28-61 have been canceled without prejudice to the filing of continuing applications. The pending claims have also been amended to reflect only elected subject matter and to correct typographical errors.

Claims 1-13 and 28-61 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enabling certain compounds under the genus. Specifically, the Examiner contends that one of ordinary skill in the art would have to engage in undue experimentation to test the different compounds within the genus of the claims in order to determine which could be used to modulate bradykinin, with no assurance of success. In applying the *Wands* factors, the crux of the Examiners argument is that "the pharmaceutical art is unpredictable" and therefore "each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity." Applicants respectfully disagree.

Initially, the Examiner contends that the instant invention is unpredictable because one of skill in the art could not determine what role modulation of bradykinin receptors plays in all disease states. Applicants believe the Examiner is misapplying this particular *Wands* factor. The current invention relates to compounds that selectively bind to the bradykinin B1 receptor *for the treatment of inflammation-related disorders*, including pain. The specification does not teach, the Applicants do not contend, and one skilled in the art should not infer from the instant application that modulation of the B1 receptor would or could play a role in the treatment of *all* diseases known to mankind, and what role it would play in any other diseases other than inflammation-related disorders. It was well known in the art at the time of the invention that bradykinin B1 receptor antagonists were useful in the treatment of inflammation (see, for example, the specification at pages 3 and 4). In fact, the nexus between the modulation of bradykinin receptors and inflammation was known well before the instant invention. For this reason, Applicants believe that the art to which the invention belongs is predictable.

Even if the art were unpredictable, the specification provides enough guidance and working examples to support the genus of compounds in the claims. As an initial matter, the specification discloses well over 70 synthesized compounds which fall within the scope of formula II and the instant claims. Further, the schemes, and in particular Scheme II, provides a

general synthetic strategy as a guide for those skilled in the art to employ, along with the actual working examples, to synthesize all the compounds of formula II. Thus, for example, where the Examiner contends that the claims are only enabled for compounds of formula II wherein C is either a 5- or 6-membered carbocyclic ring substituted in the 1 position with R', Scheme II clearly shows that 4- and 7-membered carbocyclic rings could be made by the same synthetic strategy, and that substitution at any ring position is plausible. In detail, Scheme II depicts the formation of substituted sulfonylamino-substituted bicyclic propionamides from the coupling of a β-sulfonylamino acids and the desired bicyclic-ring-substituted amine using standard peptide coupling conditions. Surely, one skilled in the art would recognize that substituting a 9- and 10-membered bicyclic amine with an 8- or 11- bicyclic amine would not alter the synthesis, since standard coupling reagents could be used in making all of these compounds. In other words, just because the working examples only teach 9- (where C is 5-membered) and 10-membered (where C is 6-membered ring) carbocyclic rings, does not mean the same chemistry could not be employed to prepare the 4- and 7-membered carbocyclic rings, and, in fact, the same chemistry could be used with great success.

Similarly, a bicyclic amine with a substitution at a position other than the 1-position, or a multiple-substituted bicyclic amine could be used as starting material for this coupling reaction. One of skill in the art would appreciate having to protect any substituents that could not withstand the reaction conditions of Scheme II and the working examples. The same argument applies for a substituent on any possible position on the phenyl ring of the C bicycle. With respect to R^a, one of skill in the art would also recognize that a secondary amine could also couple with a carboxylic acid to afford the desired bicyclic-ring amide. Thus, those compounds of formula II wherein R^a is lower alkyl and (un)substituted aryl, as well as hydrogen, are also enabled. In addition, the particular substituent at the 3-position of the starting β-sulfonylamino acid, corresponding to R^1, would also not affect the coupling reaction.

In short, the specification more than enables the compounds of the invention. The claims clearly define the boundaries of the invention, and those boundaries are aptly supported by the specification in its numerous examples and description. One skilled in the art could easily prepare the compounds of the claims, throughout their scope, by following the teachings of the specification and determine which compounds would exhibit activity for the B1 receptor in order to treat inflammation-related disorders. Therefore, one skilled in the art would not have to

engage in undue experimentation to practice the claimed invention. Withdrawal of the enablement rejection is respectfully requested.

Allowance of the claims and passage of the case to issue is respectfully solicited. Should the Examiner believe a discussion of this matter would be helpful, she is invited to telephone the undersigned at (312) 913-0001.

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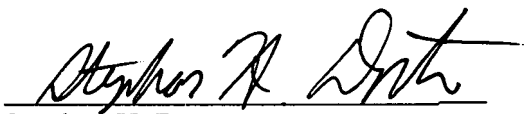
By: 

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